("Zhang") in view of Lee *et al*, (CA 124:105153, abstract of J. Microcolumn Sep. (1995), 7(5), 477-83) ("Lee"). (Paper No. 15 at 3.)

For the reasons set forth below the rejection, respectfully is traversed.

Zhang discloses "HPLC determination of vitamin D_3 preparation." (Title). The Abstract relied on by the rejection recites the following:

> In the column system suitability test following irradn. of heated vitamin D_3 soln. by UV with main wave length 254 and 365 nm for 5 min, 6 isomers were sepd. with the normal-phase HPLC (Waters Resolve Silica column, 0.3% n-pentanol in hexane as mobile phase, detected at 254 nm), with resoln. factor, R, >1.0. The linearity was obtained in 0.5-60 .mu.g vitamin D_3. The low concn. (1ppm) prepn. could be detd. by internal (di-Me phthalate) method or external (thermal equil.) method with error 10%. The error in detn. of high-concn. prepn. was 3%.

(Abstract).

Lee discloses the use of an "enhanced liquidity" or a low viscosity liquid mobile phase as an eluent in reversed phase HPLC. (Page 477, Col. 1). In Lee, "***all***" experiments disclosed were performed using a 0.7/0.30 mole fraction methanol/H_2O mixture or a 0.49/0.21/0.30 mole fraction methanol/H_2O/CO_2 mixture. (Page 478, Col. 1). Lee further discloses that "***[r]eversed phase HPLC, <u>unlike</u> normal phase HPLC and SFC*** (supercritical fluid chromatography), ***is the <u>only</u> technique by which vitamins D_2 ... and D_3 ... can be resolved***." (Page 482, Col. 2). In Figure 5, Lee presents a chromatogram of fat soluble vitamins, including vitamin D_3, and concludes that the separation "is attributed to the ... ***reversed phase conditions***." (*Id.*).

In making the rejection, the Examiner asserted that Zhang teaches "the separation of 6 isomers separated by using irradiation technique and the purification on silica column (stationary phase)." (Paper No. 15 at 3). The Examiner acknowledged, however, that the

"instant claims differ from the [Zhang] in claiming the liquid CO_2 for separation by column chromatography using liquid CO_2." (*Id.*) To fill the acknowledged gap, the Examiner relied upon Lee as teaching "the separation of coal tar vitamins and other related compounds ... [the enhanced] fluidity liquid mobile phase containing CO_2/methanol/water are used in a column." (*Id.*).

The Examiner then asserted that the "references are combinable because they are from the same field of endeavor." (*Id.*). The Examiner then contended that "it would have been obvious to one skilled in the art to combine the teachings of prior art supra to separate the vitamin D derivatives particularly when Zhang *et al.* teaches irradiation technique and the purification on silica column (stationary phase) and Lee *et al.* teaches the use of liquid CO_2 for separation." (*Id.*) The Examiner further contended that "***ample motivation***" for separating vitamin D_3 as claimed is found in the prior art, and that there was "***nothing unobvious***" about the process for separating the vitamin D_3 as claimed. (*Id.* at 4.)

As noted in our earlier Response to Office Action Including Amendment and Petition for Extension of Time dated October 3, 2000 ("earlier Response"), the rejection uses the wrong standard for determining obviousness. The Examiner continues to propound a rejection relying upon "***ample motivation***" (*Id.*), "***nothing unobvious***" (*Id.*), and "***reasonably infer***" (*Id.* at 5) standards that are not found in the statute or precedential authority. Further, the Examiner has failed to address this deficiency in Paper No. 15. Accordingly, we are compelled to reiterate the arguments made in our earlier Response.

Reliance on such novel standards for a §103(a) rejection, *e.g.*, that there is "nothing unobvious" recited in the claim is simply improper. It is the Examiner's burden to set

forth evidence sufficient to support a case of *prima facie* obviousness - not to make unsupported conclusions that there is "nothing unobvious" about the claim.

Similarly, whether or not "ample motivation" is found in the prior art to combine references, it is the Examiner's burden to explain with particularity where the motivation to combine ***and*** where the reasonable expectation of success are found. As is fundamental, a *prima facie* case of obviousness must be based on facts, "cold hard facts." *In re Freed*, 165 USPQ 570, 571-72 (C.C.P.A. 1970). When the rejection is not supported by facts, it cannot stand. *Ex parte Saceman*, 27 USPQ2d 1472, 1474 (B.P.A.I. 1993). A mere invocation of the "prior art" without reference to the particular document(s) relied on is insufficient to support a conclusion of obviousness under §103(a).

As is well settled, an Examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force which would ***impel*** one skilled in the art to do what the patent applicant has done. *Ex parte Levengood*, 28 USPQ2d 1300, 1301-02 (BPAI 1993). "Reasonably infer," just like "ample motivation" and "nothing unobvious," is simply not the standard on which conclusions of obviousness may be based. In sum, the rejection fails to provide any reason ***why*** one would be motivated, let alone impelled, to combine the references in the manner suggested by the Examiner. In short, the rejection fails to meet its burden because it relies on the wrong legal standards. And, thus it should be withdrawn.

Even if the rejection is deemed to be founded on the correct legal standard, it fails to state sufficient facts to support a *prima facie* case of obviousness.

The Examiner's attention is drawn to the Preliminary Amendment filed concurrently with the Continuing Prosecution Application on February 6, 2001. Claim 1 as

amended recites the use of "a ***normal phase chromatographic technique***." Once again, the Examiner has not addressed the arguments made in our earlier Response.

First, Lee explicitly discloses that ***reversed phase HPLC is the only technique by which, e.g. vitamin D_3 can be resolved***. (Page 482, Col. 2 and Figure 5). Lee attributes this ability to separate, *e.g.* vitamin D_3, to the "***reversed phase*** conditions." (*Id.*).

It is well settled that it is improper to combine references where the references teach away from their combination. *See* MPEP §2145 at 2100-123 and *In re Grasselli*, 218 USPQ 769, 779 (Fed. Cir. 1983). Here, Lee specifically discloses that the ***reversed phase*** system succeeded in resolving vitamin D_3 where both normal phased and supercritical fluid HPLC had failed. (Page 482, Col. 2). Thus, the "teachings" of Zhang and Lee clearly conflict. Accordingly, the Examiner had the burden to determine how one of skill in this art would resolve such a conflict. *See* MPEP §2143.01 at 2100-98 ("Where the teachings of two or more prior art references conflict, the Examiner ***must*** weigh the power of each reference to suggest solutions to one of skill in the art ...."). This the rejection has not done. Thus for this additional reason, the rejection should be withdrawn.

Second, a *prima facie* case of obviousness requires that the rejection describe with specificity ***why*** one skilled in the art would have combined the references to arrive at the claimed invention. *In re Dembiczak*, 50 USPQ2d 1614, 1617 (CAFC 1999). ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of *the requirement for a showing of the teaching or motivation to combine prior art references*."). *See also In re Kotzab*, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). ("[A] rejection cannot be predicated on the mere identification ... of individual components of claimed limitations. Rather, ***particular findings must be made*** as to the reason the skilled

artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.")

Here, the rejection contains no such explanation or particular findings of fact. The rejection completely ignores Lee's "teaching away" without providing a scintilla of evidence to explain why one skilled in this art would ignore the express disclosure of Lee that only a reversed phase HPLC process would separate, *e.g.* vitamin D_3. Instead, the rejection uses the present specification as a blue print to interpret the disparate disclosures of Zhang and Lee, and in doing so has fallen into the same "hindsight trap" as the Examiner and Board did in *Kotzab*. (*Id.* at 1318). For this additional reason, the rejection should be withdrawn.

In sum, because the rejection provides no evidence or reasoning to explain why one should ignore the express teaching of Lee, the rejection is left with the acknowledged gap (*i.e.*, no teaching of a liquid or supercritical CO_2 for the mobile phase) that it cannot fill based on the evidence and reasoning set forth in the rejection.

Also, as noted in our earlier Response, the rejection relies on Zhang, which is an abstract that is so factually incomplete that it cannot be used in the manner suggested by the Examiner.

Zhang recites a "column suitability test." The rejection, however fails to provide any explanation of how a ***column suitability test*** relates to a ***process for isolating*** vitamin D_3 or previtamin D_3 as claimed. Moreover, Zhang states that 6 isomers were separated ("sepd.") with normal phase HPLC. The rejection assumes, without a shred of evidence, that the "6 isomers" recited in Zhang refer to isomers of vitamin D_3 or previtamin D_3 as recited in claim 1.

Zhang concludes by presenting percent error in ***detection*** ("detd.") data of some substance (whether a specific compound or mixture of 6 isomers is not clear) in a high

concentration preparation (3% error) and a low concentration preparation (10% error). The rejection, however, fails to explain how a method of ***detection*** relates in any way to the presently claimed process for ***isolating*** vitamin D_3 or previtamin D_3.

Thus, the rejection reads into Zhang a number of elements recited by the present claims without providing any evidence or reasoning for doing so. In the absence of such evidence, it can only be concluded that the present specification was used as the template to fill in the factual gaps noted above with respect to Zhang. But this type of hindsight reconstruction is expressly prohibited. *In re Dow Chem. Co.*, 5 USPQ2d 1529, 1531-1532 (Fed. Cir. 1988) ("There ***must*** be a reason or suggestion in the prior art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure."). For this additional reason, the rejection should be withdrawn.

Accordingly, for the reasons set forth above, reconsideration, withdrawal of the rejections, and allowance of the claims is respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231, on July 9, 2001.

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Respectfully submitted,

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